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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,645	11/13/2001	Menzo Jans Emco Havenga	5006.1US	4875
24247	7590	08/19/2004	EXAMINER	
TRASK BRITT P.O. BOX 2550 SALT LAKE CITY, UT 84110			MARVICH, MARIA	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 08/19/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/010,645	Applicant(s) HAVENGA ET AL.	
	Examiner Maria B Marvich, PhD	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49 and 51-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 49 and 51-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to an After-Final Amendment filed 7/20/04. **The amendment has been entered.** Claims 1-48 and 50 have been cancelled. Claim 49 has been amended. Claims 49 and 51-61 are pending. Upon further review of the instant claims and specification it is apparent that the application is not in condition for allowance. Therefore, prosecution is reopened. As new grounds of rejection are presented in this action that are not necessitated by applicant's amendment of the claims, this action is non-final.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 49 and 51-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claim 49 is vague and indefinite in that the metes and bounds of "fiber protein of a second adenovirus serotype associated therewith" are unclear. It is unclear to what "associated therewith" is referring.

Claim 49 is vague and indefinite in that the metes and bounds of "infecting the mesenchymal stem cell with the recombinant adenovirus (rAd)" are unclear. Are the cells transduced twice with rAd- once by administration and a second time by infection? If so, what steps are encompassed by the step of "infecting" the cells with the rAd that are not encompassed by the step of "administering"? Or does administering of the

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administration encompass the step of infecting the cells? If this is the case, it is redundant to recite that the cells are administered and infected with rAd, as infection is a natural process that results from administration.

Claim 54 is vague and indefinite in that the metes and bounds of “the tropism determining part of the fiber protein is selected from the group” are unclear. The claim recites that the fiber protein is selected from a group of adenoviral serotypes and as such is unclear. The fiber protein cannot be selected from a serotype but rather from a group of fiber proteins. It would be remedial to recite “is selected from the fiber proteins from adenovirus of the group consisting of serotype 16, serotype 32, serotype 35, serotype 40-S and serotype 51”.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Applicants' recite a recombinant adenovirus with tropism for mesenchymal stem cells (MSC). The recombinant adenovirus has a fiber protein with a tropism determining

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combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

Applicants recite a broad genus of "tissue determining parts" and "tail regions" and knob regions" of a fiber from a second adenovirus serotype. In the instant case, applicants describe the tropism-determining component of the fiber to be located in the "knob protein" and that the first 30 amino acids. The sequences of the "tissue determining parts" are not provided. The tail functions to anchor the fiber to the penton base (page 10, paragraph 0038) but a "tail region" is not described. The knob is described as mediating tropism and experiments are described in which insertions into the fiber HI loop result in retargeting. However, no "knob regions" are so described. In practice, the entire fiber from adenovirus serotypes 16, 32, 35, 40-S and 51 is required to increase MSC tropism. Specifically, a recombinant adenovirus is constructed from a vector, pBr/Ad.BamRΔFib, deleted of the entire adenovirus 5 fiber sequence (see e.g. paragraph 0091). Fiber sequences are amplified from a variety of adenovirus such as serotypes 16, 32, 35, 40-S and 51 and inserted into the fiber-deleted vector. In fact the specification teaches, "(I)t is preferred to use a whole fiber protein of an adenovirus comprising such a part of the fiber of Ad16" (see page 3, paragraph 0011).

Therefore, applicants do not describe the structure of a "tissue tropism determining part" or "tail regions" or "knob regions" such that one of skill in the art could envision the sequences of the fiber that are required to provide tissue tropism for mesenchymal cells. Applicants do not disclose relevant identifying characteristics of "tropism determining part" of the fiber protein, "a tail region" or "a knob region" such that a person of skill in the art could envision the recited sequences. The specification

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specification teaches, “(I)t is preferred to use a whole fiber protein of an adenovirus comprising such a part of the fiber of Ad16” (see page 3, paragraph 0011).

Therefore, applicants do not describe the structure of a “tissue tropism determining part” or “tail regions” or “knob regions” such that one of skill in the art could envision the sequences of the fiber that are required to provide tissue tropism for mesenchymal cells. Applicants do not disclose relevant identifying characteristics of “tropism determining part” of the fiber protein, “a tail region” or “a knob region” such that a person of skill in the art could envision the recited sequences. The specification fails to reduce to practice or provide clear depiction of properties or structures of “tissue tropism determining parts” or “tail regions” or “knob regions” required for generation of the recited recombinant adenovirus fiber proteins. Therefore, the specification fails to describe the requirements of the fiber such that a structure-function nexus is readily apparent to the skilled artisan and the relevant identifying characteristics are unknown. In an unpredictable art, the disclosure of one species would represent to the skilled artisan a lack of a representative number of species sufficient to show applicants were in possession of claimed genus. Given the diversity of protein fragments of an adenovirus serotype of subgroup C and the lack of written disclosure of the structural characteristics, and the lack of written disclosure of the functional characteristics required of the fragment for fiber production in a chimeric fiber, it is concluded that applicant was not in possession of their invention.

Conclusion

No claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

August 10, 2004


DAVID GUZO
PRIMARY EXAMINER